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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,626	08/04/2006	Philip Savage	30699/42250	7227

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,626	SAVAGE, PHILIP	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *14-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-6-06&2-25-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-13, in the reply filed on 4-30-08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14-37 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4-30-08.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to a method of damaging target cells in a subject, the method comprising administering to the subject: 1) a nucleic acid encoding portion of alcohol dehydrogenase (ADH) that converts ethanol to acetaldehyde; and 2) ethanol.

While the claims do not require therapy, the sole disclosed purpose for administering a nucleic acid encoding alcohol dehydrogenase and ethanol to a subject is treatment (pg 1, lines 6-13). The enablement rejection does not conflict with the art rejections because the art rejections are based on the claims, which do not require treatment. The enablement rejection is based on how to use the method claimed to treat disease in a subject. If other enabled uses for the method claimed besides treatment are disclosed, please point to them by page and line number.

At the time of filing Greco (J. Cellular Physiology, 2001, Vol. 187, pg 22-36) taught gene directed enzyme prodrug therapy (GDEPT) was known in the art by administering a vector encoding an enzyme of choice into tumor cells along with the enzyme's substrate that is converted into a toxic substance, which causes cell death (pg 23, Fig. 1). Using adenovirus for this type of treatment was known in the art at the time of filing (pg 28, 2nd full paragraph, last sentence; pg 28, col. 2, line 16, for example), and the promoter may be tumor-selective (pg 28, col. 1, 2nd full paragraph, line 5). Greco taught problems with gene therapy included delivery of a gene to the tumor, regulation of gene expression and therapeutic efficiency (pg 22, col. 1). All of the GDEPT described by Greco require direct injection into the tumor (see entire article); however, the claims at hand encompass any route of injection. Greco describes the desired features of the enzyme/prodrug combination on pg 23 and states several

combinations have been proposed for GDEPT, but most of them do not fulfill all the requirements including those in clinical trials (col. 2). Thus, it was unpredictable how to obtain a therapeutic effect using GDEPT at the time of filing.

The specification teaches administering transfected tumor cells then administered ethanol to mice (pg 61). The transfected tumor cells did not grow as fast as non-transfected tumor cells. Different cytotoxic effects were obtained depending upon the number of cells used (Fig. 1 vs. Fig. 2).

The specification teaches accurate assessment of cytotoxic effects of exposure to acetaldehyde is extremely difficult in vitro because acetaldehyde is volatile and because cells are able to metabolize acetaldehyde resulting in more rapid reductions in acetaldehyde dependant on the type and number of cells present (pg 63, lines 16-21).

The specification suggests using the method for treatment in vivo (pg 65-68) but does not teach how much ADH expression, ethanol or acetaldehyde are required to treat a pre-existing tumor or how to administer the nucleic acid in the absence of cells to obtain the same toxicity. Given the unpredictability of gene therapy in the art at the time of filing, taken with the teachings in the specification, it would have required those of skill undue experimentation to determine the parameters required to damage target cells in vivo using 1) a nucleic acid sequence encoding ADH and 2) ethanol as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Mapoles (Alcoholism: Clinical and Exp. Res., May/June 1994, Vol. 18, No. 3, pg 632-639).

Mapoles introduced a plasmid encoding full length alcohol dehydrogenase (ADH) into a culture of cells and damaged cells expressing ADH when exposed to alcohol (pg 632-634, "Materials and Methods", specifically pg 634, col. 1, "Analysis of pSV2ADH in CHO cells"). Acetaldehyde exposure inhibited growth of the cells (title). The "subject" claimed is the cell culture and the "target cells" are those expressing ADH.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-9 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Philipott (Cancer Res. June 1979, Vol. 39, pg 2084-2089) in view of Greco (J. Cellular Physiology, 2001, Vol. 187, pg 22-36) and Yokoyama (Biochem. Biophys. Res. Communications, Aug. 30, 1994, Vol. 203, No. 1, pg 219-224).

Philipott administered alcohol dehydrogenase (ADH) antibody directed enzyme producing therapy (ADEPT) to tumor cells. ADH was covalently conjugated to anti-trinitrophenyl (TNP) antibody. The cells were cultured with allyl alcohol (AA) (pg 2085, col. 2, last full paragraph, "AA (Fisher Scientific..."; pg 2084, col. 1, footnote of abbreviations, "AA, allyl alcohol"). Philipott did not teach administering the ADH as gene directed enzyme producing therapy (GDEPT).

However, GDEPT was well known in the art as described by Greco who taught treating cancer by administering a vector encoding an enzyme of choice into tumor cells along with the enzyme's substrate that is converted into a toxic substance, which causes cell death (pg 23, Fig. 1). Using adenovirus for this type of treatment was well

known in the art at the time of filing (pg 28, 2nd full paragraph, last sentence; pg 28, col. 2, line 16, for example). The promoter may be tumor-selective (pg 28, col. 1, 2nd full paragraph, line 5), which is "target cell-specific promoter" (claim 7) and a "target cell-specific portion" (claim 9). Claim 11 is included because the metes and bounds of "capable of selectively binding to a cell surface entity" because the metes and bounds of "target-cell specific portions" of a vector having that function are indefinite (see 112/2nd).

Furthermore, the nucleic acid sequence of ADH was well known in the art at the time of filing as supported by Yokoyama, for example.

Thus it would have been obvious to those of ordinary skill in the art at the time of filing to direct alcohol dehydrogenase (ADH) to tumor cells in combination with alcohol as described by Philipott, wherein the ADH was directed to tumor cells using GDEPT, i.e. using DNA encoding ADH as described by Greco. Antitumor gene therapy was described in the art at the time of filing as providing "highly specific gene delivery" and "highly specific gene expression" (pg 22, col. 1, paragraph 1, line 5). Specific gene expression and prodrug activation offer the possibility of combining GDEPT systems to enhance the antitumor activity of single treatments without increasing systemic toxicity (pg 27, 11 lines from the end). Thus, those of ordinary skill in the art would have been motivated to replace ADH with the DNA encoding ADH to be able to target tumor cells more specifically using a tumor specific promoter such as the erbB-2 promoter described by Greco (pg 28, col. 1, paragraph 2, line 5).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner